Figure 1

A. Rig open reading frame nucleotide sequence

atgccggaacagagtaacgattaccgcgtggtggtgttcggggcgggcggcgtgggcaag
agctcgctggtgctgcgcttcgtgaagggcacgttccgcgacacctacatccccaccatc
gaggacacctaccggcaggtgatcagctgcgacaagagcgtGtgcacgctgcagatcaca
gacaccaccggcagccaccagttcccggccatgcagcgcctgtccatctccaagggccac
gccttcatcctggtgttctccgtcaccagcaagcagtcgctggaggagctggggcccatc
tacaagctcatcgtgcagatcaagggcagcgtggaggacatccccgtgatgctcgtgggc
aacaagtgcgatgagacgcagcgggaggtggacacgcgcgaggcgcaggcggtggcccag
gagtggaagtgcgctttcatggagacctcggccaagatgaactacaacgtcaaggagctc
ttccaggagctgctgacgctggagacgcgccggaacatgagcctcaacatcgacggcaag
cgctccgggaagcagaagaggacagaccgcgtcaagggcaaatgcaccctcatgtga

B. Rig amino acid sequence

MPEQSNDYRVVVFGAGGVGKSSLVLRFVKGTFRDTYIPTIEDTYRQVISCD
KSVCTLQITDTTGSHQFPAMQRLSISKGHAFILVFSVTSKQSLEELGPIYKLIV
QIKGSVEDIPVMLVGNKCDETQREVDTREAQAVAQEWKCAFMETSAKMN
YNVKELFQELLTLETRRNMSLNIDGKRSGKQKRTDRVKGKCTLM

Figure 2

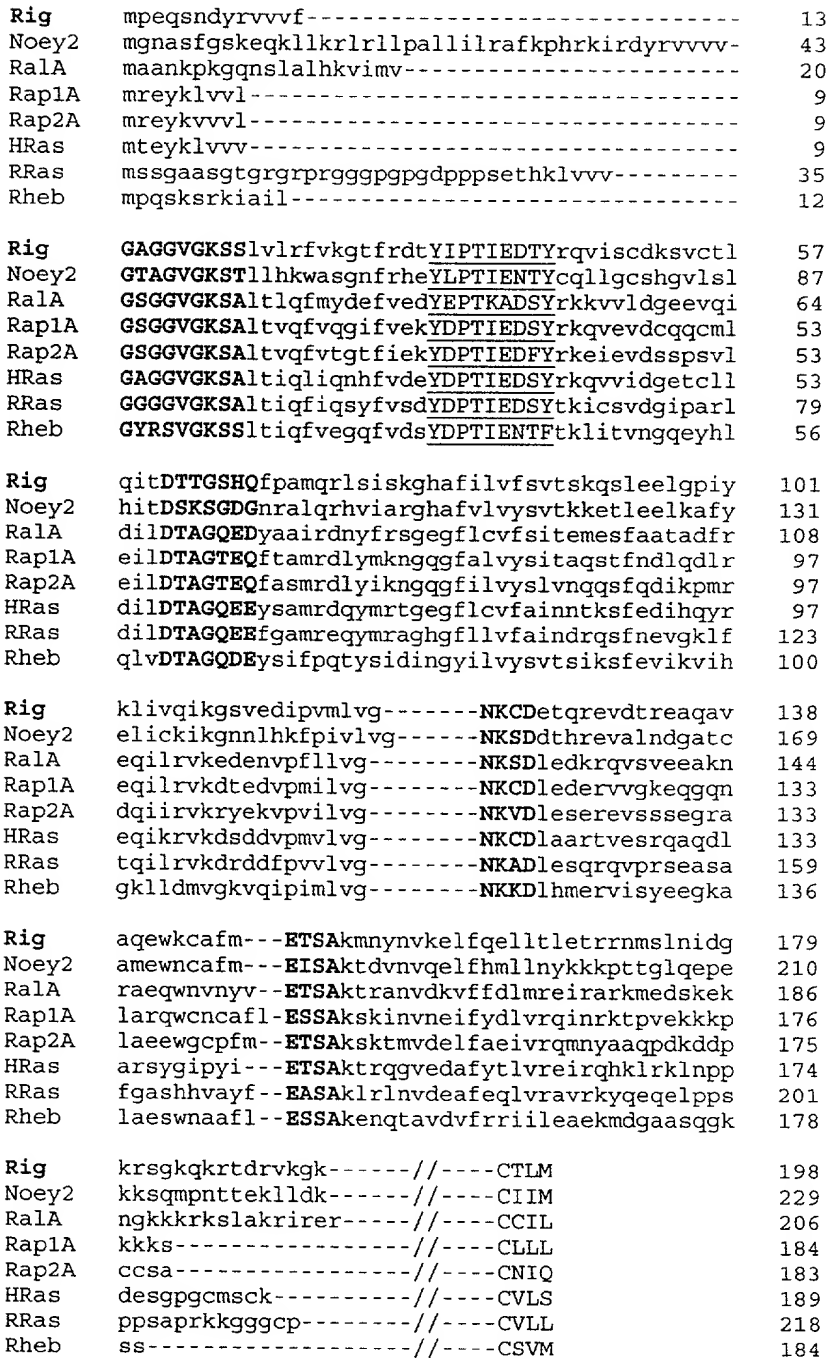

Rig mpeqsndyrvvvf---------- 13
Noey2 mgnasfgskeqkllkrlrllpallilrafkphrkirdyrvvvv- 43
RalA maankpkgqnslalhkvimv---------- 20
Rap1A mreyklvvl---------- 9
Rap2A mreykvvvl---------- 9
HRas mteyklvvv---------- 9
RRas mssgaasgtgrgrprgggpgpgdpppsethklvvv--------- 35
Rheb mpqsksrkiail---------- 12
Rig GAGGVGKSSlvlrfvkgtfrdtYIPTIEDTYrqviscdksvctl 57
Noey2 GTAGVGKSTllhkwasgnfrheYLPTIENTYcqllgcshgvlsl 87
RalA GSGGVGKSAltlqfmydefvedYEPTKADSYrkkvvldgeevqi 64
Rap1A GSGGVGKSAltvqfvqgifvekYDPTIEDSYrkqvevdcqqcml 53
Rap2A GSGGVGKSAltvqfvtgtfiekYDPTIEDFYrkeievdsspsvl 53
HRas GAGGVGKSAltiqliqnhfvdeYDPTIEDSYrkqvvidgetcll 53
RRas GGGGVGKSAltiqfiqsyfvsdYDPTIEDSYtkicsvdgiparl 79
Rheb GYRSVGKSSltiqfvegqfvdsYDPTIENTFtklitvngqeyhl 56
Rig qitDTTGSHQfpamqrlsiskghafilvfsvtskqsleelgpiy 101
Noey2 hitDSKSGDGnralqrhviarghafvlvysvtkketleelkafy 131
RalA dilDTAGQEDyaairdnyfrsgegflcvfsitemesfaatadfr 108
Rap1A eilDTAGTEQftamrdlymkngqgfalvysitaqstfndlqdlr 97
Rap2A eilDTAGTEQfasmrdlyikngqgfilvyslvnqqsfqdikpmr 97
HRas dilDTAGQEEysamrdqymrtgegflcvfainntksfedihqyr 97
RRas dilDTAGQEEfgamreqymraghgfllvfaindrqsfnevgklf 123
Rheb qlvDTAGQDEysifpqtysidingyilvysvtsiksfevikvih 100
Rig klivqikgsvedipvmlvg-------NKCDetqrevdtreaqav 138
Noey2 elickikgnnlhkfpivlvg------NKSDdthrevalndgatc 169
RalA eqilrvkedenvpfllvg--------NKSDledkrqvsveeakn 144
Rap1A eqilrvkdtedvpmilvg--------NKCDledervvgkeqgqn 133
Rap2A dqiirvkryekvpvilvg--------NKVDleserevsssegra 133
HRas eqikrvkdsddvpmvlvg--------NKCDlaartvesrqaqdl 133
RRas tqilrvkdrddfpvvlvg--------NKADlesqrqvprseasa 159
Rheb gklldmvgkvqipimlvg--------NKKDlhmervisyeegka 136
Rig aqewkcafm---ETSAkmnynvkelfqelltletrrnmslnidg 179
Noey2 amewncafm---EISAktdvnvqelfhmllnykkkpttglqepe 210
RalA raeqwnvnyv--ETSAktranvdkvffdlmreirarkmedskek 186
Rap1A larqwcncafl-ESSAkskinvneifydlvrqinrktpvekkkp 176
Rap2A laeewgcpfm--ETSAksktmvdelfaeivrqmnyaaqpdkddp 175
HRas arsygipyi---ETSAktrqgvedafytlvreirqhklrklnpp 174
RRas fgashhvayf--EASAklrlnvdeafeqlvravrkyqeqelpps 201
Rheb laeswnaafl--ESSAkenqtavdvfrriileaekmdgaasqgk 178
Rig krsgkqkrtdrvkgk------//----CTLM 198
Noey2 kksqmpntteklldk------//----CIIM 229
RalA ngkkkrkslakrirer-----//----CCIL 206
Rap1A kkks----------//----CLLL 184
Rap2A ccsa----------//----CNIQ 183
HRas desgpgcmsck----------//----CVLS 189
RRas ppsaprkkgggcp--------//----CVLL 218
Rheb ss----------//----CSVM 184

Figure 3

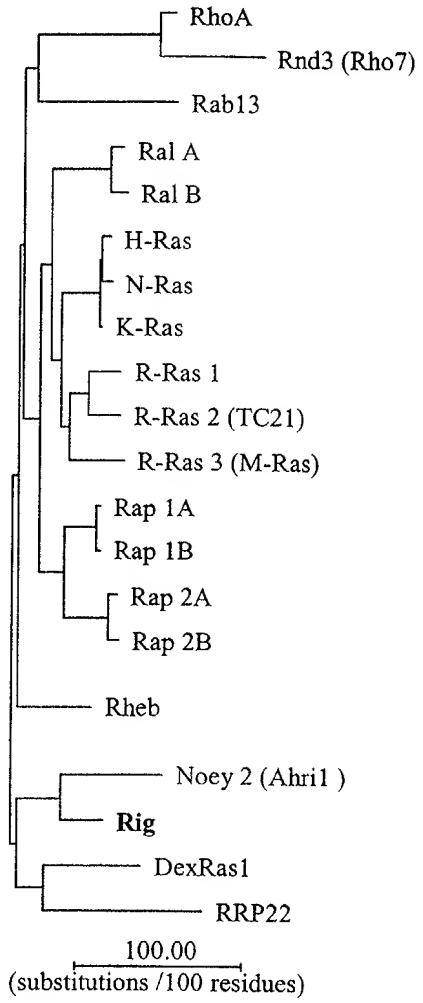
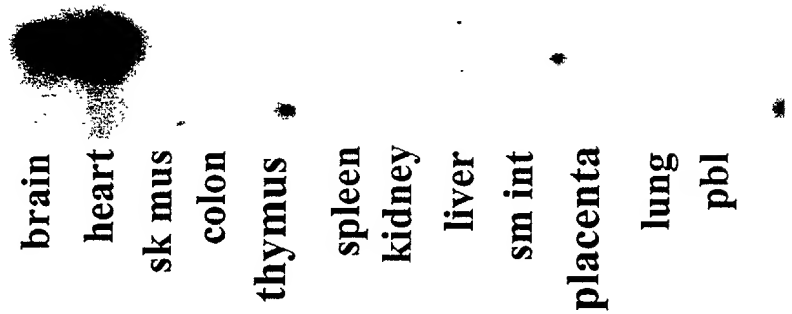
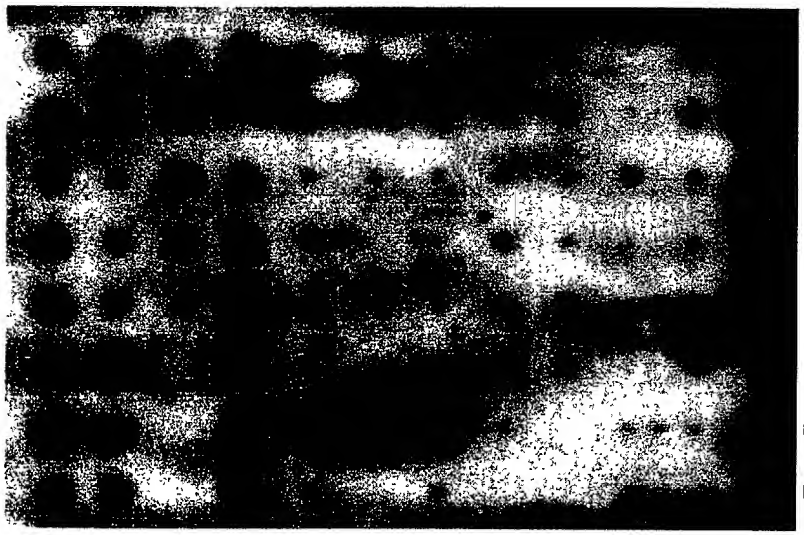

RhoA
Rnd3 (Rho7)
Rab13
Ral A
Ral B
H-Ras
N-Ras
K-Ras
R-Ras 1
R-Ras 2 (TC21)
R-Ras 3 (M-Ras)
Rap 1A
Rap 1B
Rap 2A
Rap 2B
Rheb
Noey 2 (Ahri1)
Rig
DexRas1
RRP22
100.00
(substitutions /100 residues)

Figure 4

(A)



(B)



(C)

	1	2	3	4	5	6	7	8	9	10	11	12
A	whole brain	cerebellum, left	substantia nigra	heart	esophagus	colon, transverse	kidney	lung	liver	leukemia, HL-60	fetal brain	yeast total RNA
B	cerebral cortex	cerebellum, right	nucleus accumbens	aorta	stomach	colon, descending	skeletal muscle	placenta	pancreas	HeLa S3	fetal heart	yeast tRNA
C	frontal lobe	corpus callosum	thalamus	atrium, left	duodenum	rectum	spleen	bladder	adronal gland	leukemia, K-562	fetal kidney	*E. coli* rRNA
D	parietal lobe	amygdala	pituitary gland	atrium, right	jejunum		thymus	uterus	thyroid gland	leukemia, MOLT-4	fetal liver	*E. coli* DNA
E	occipital lobe	caudate nucleus	spinal cord	ventricle, left	ileum		peripheral blood leukocyte	prostate	salivary gland	Burkitt's lymphoma, Raji	fetal spleen	poly r(A)
F	temporal lobe	hippo-campus		ventricle, right	ileocecum		lymph node	testis	mammary gland	Burkitt's lymphoma, Daudi	fetal thymus	human C_0t -1 DNA
G	p. g.* of cerebral cortex	medulla oblongata		inter-ventricular septum	appendix		bone marrow	ovary		colorectal adeno-carcinoma, SW480	fetal lung	human DNA 100 ng
H	pons	putamen		apex of the heart	colon, ascending		trachea			lung carcinoma, A549		human DNA 500 ng

* paracentral gyrus

Figure 5

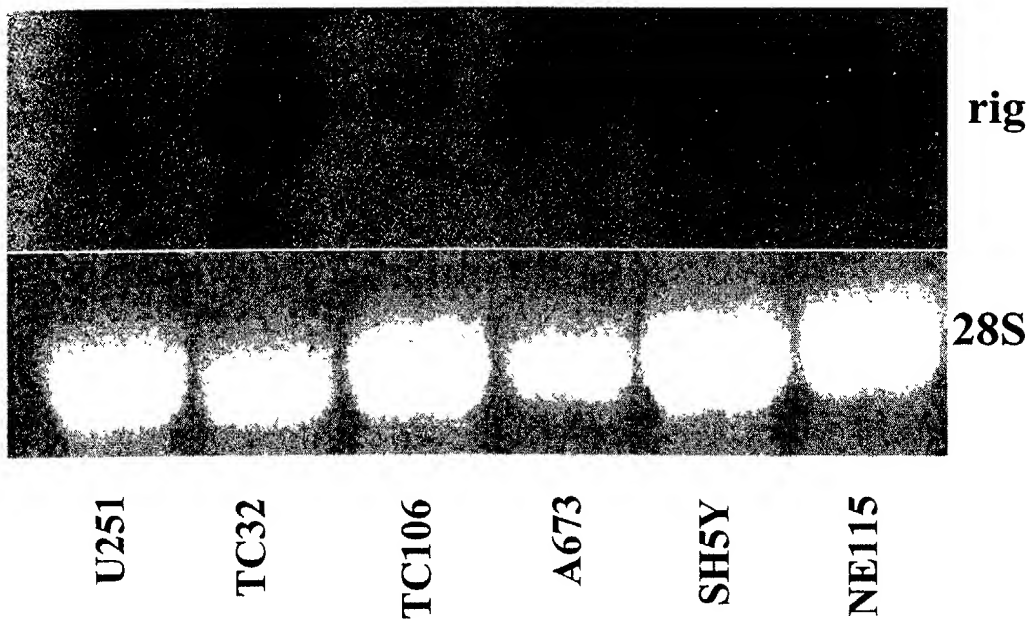


Figure 6

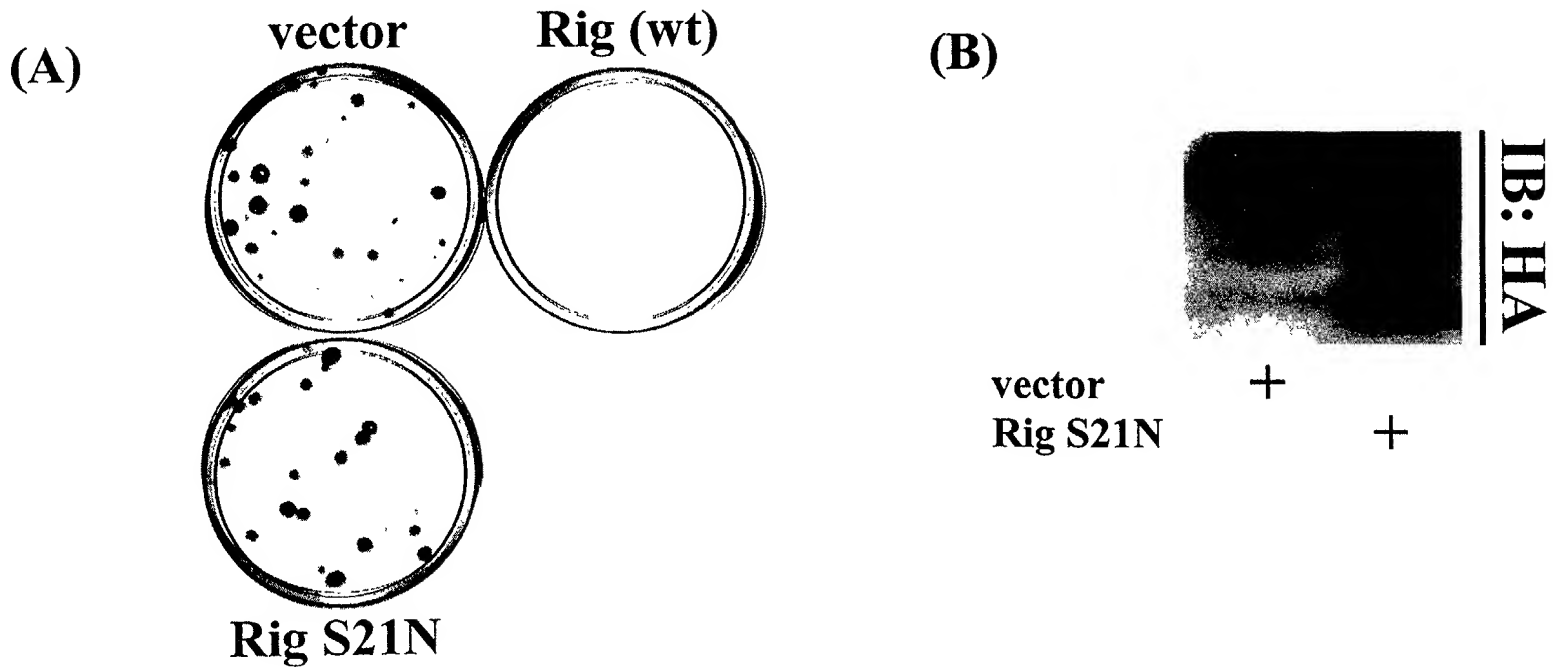


Figure 7

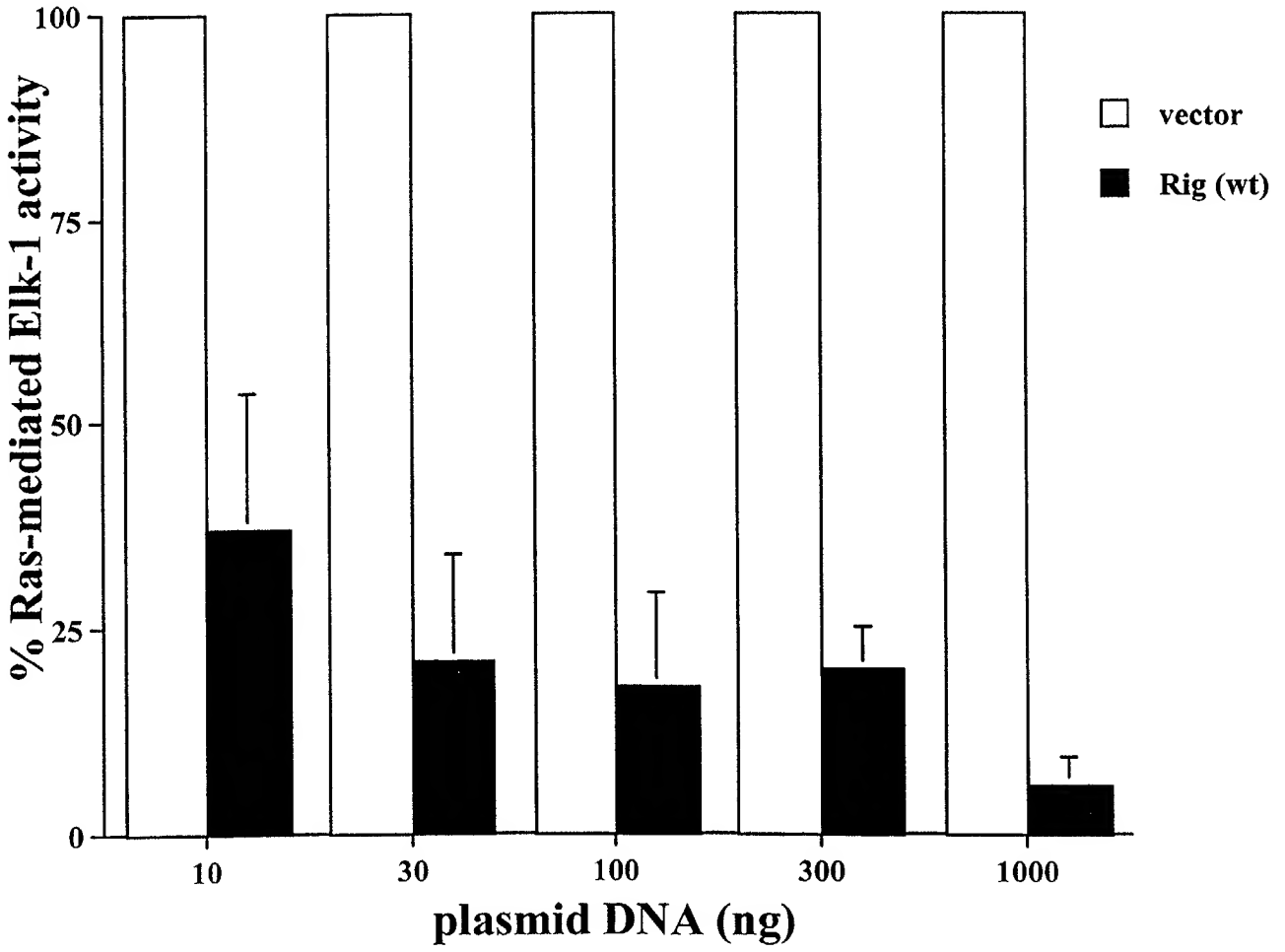


Figure 8

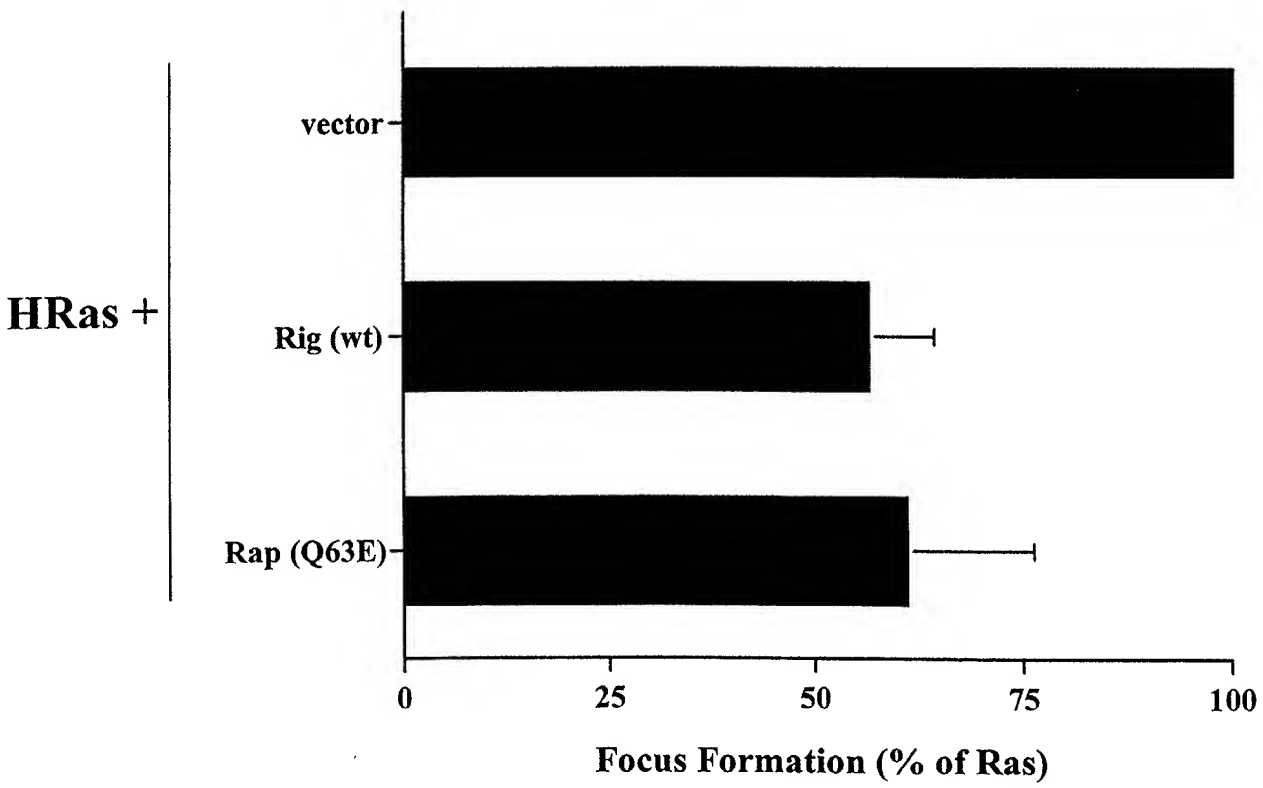
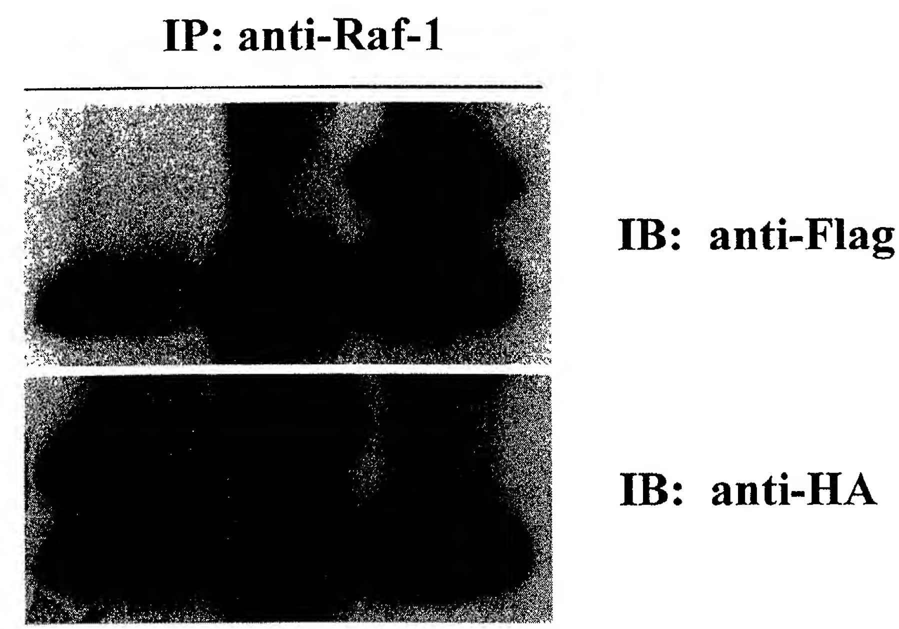

HRas +
vector
Rig (wt)
Rap (Q63E)
0
25
50
75
100
Focus Formation (% of Ras)

Figure 9



HA-Raf-1	+	+	+
FLAG-Rig			+
HA-H-Ras	+		
HA-K-Ras		+	

Figure 10

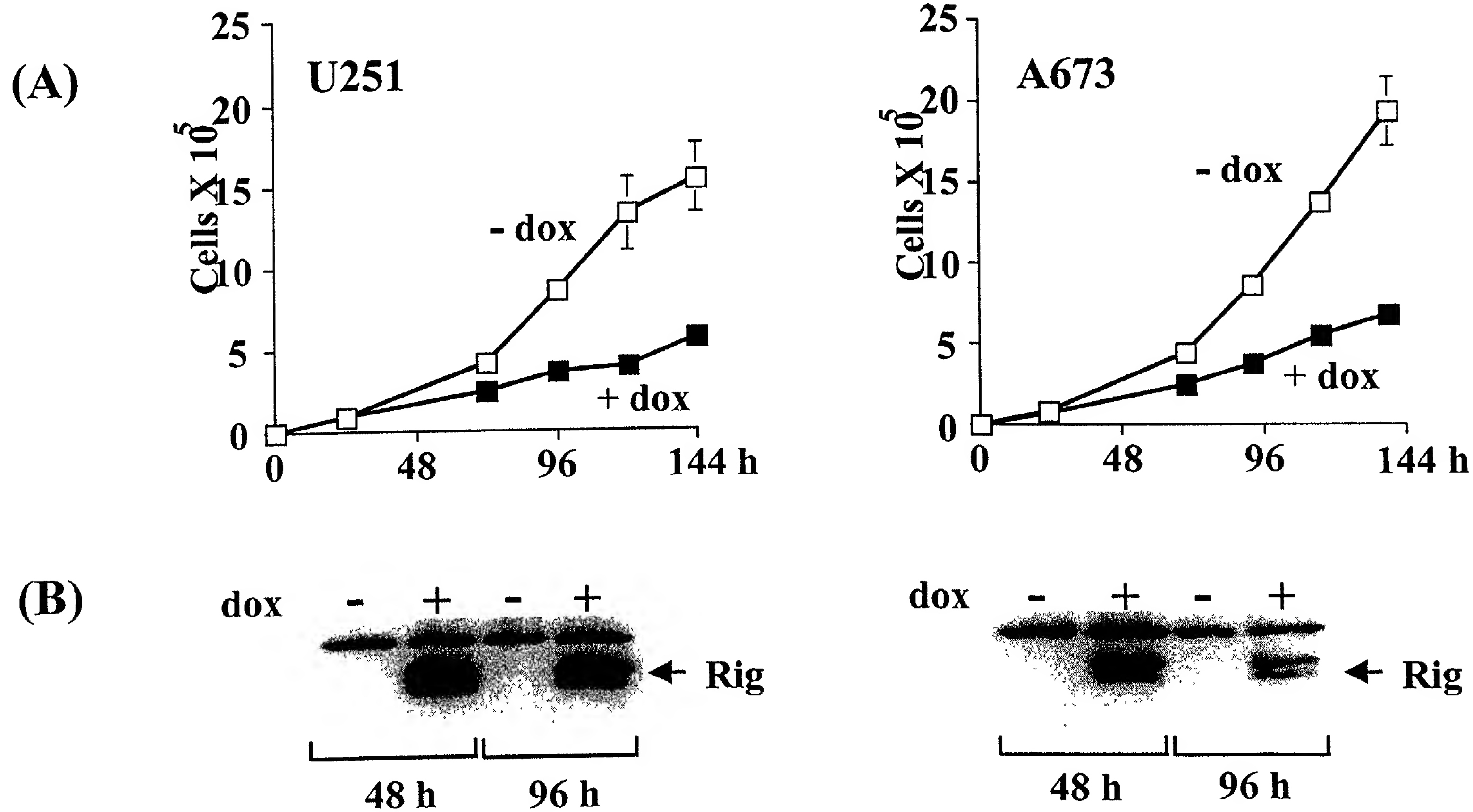

(A)
U251
A673
Cells X 10^5
25
20
15
10
5
0
0
48
96
144 h
- dox
+ dox
(B)
dox
-
+
-
+
Rig
48 h
96 h

Figure 11

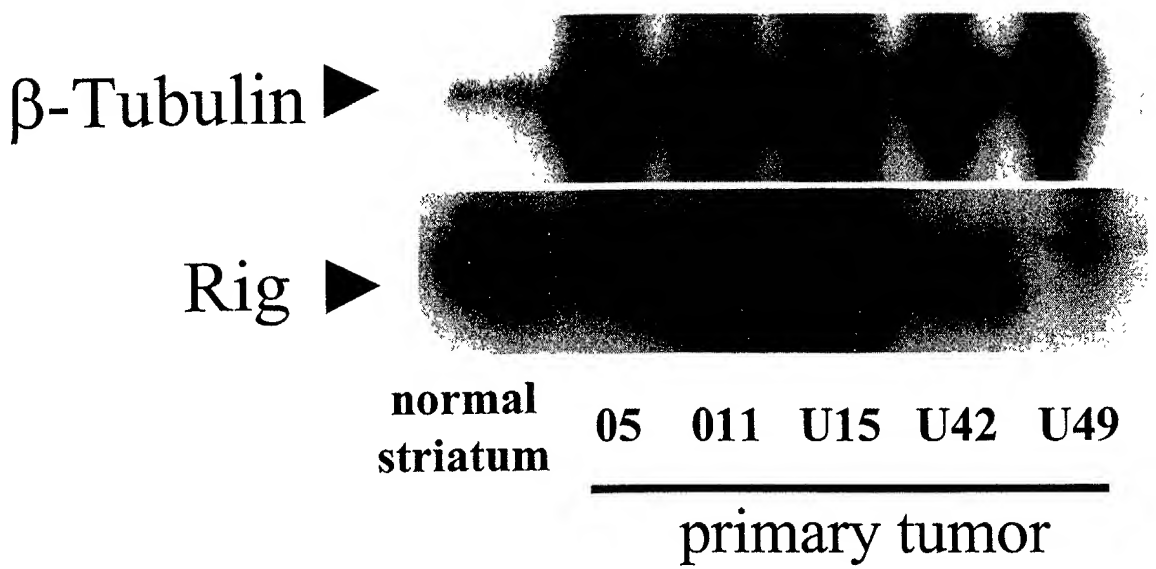


Figure 12

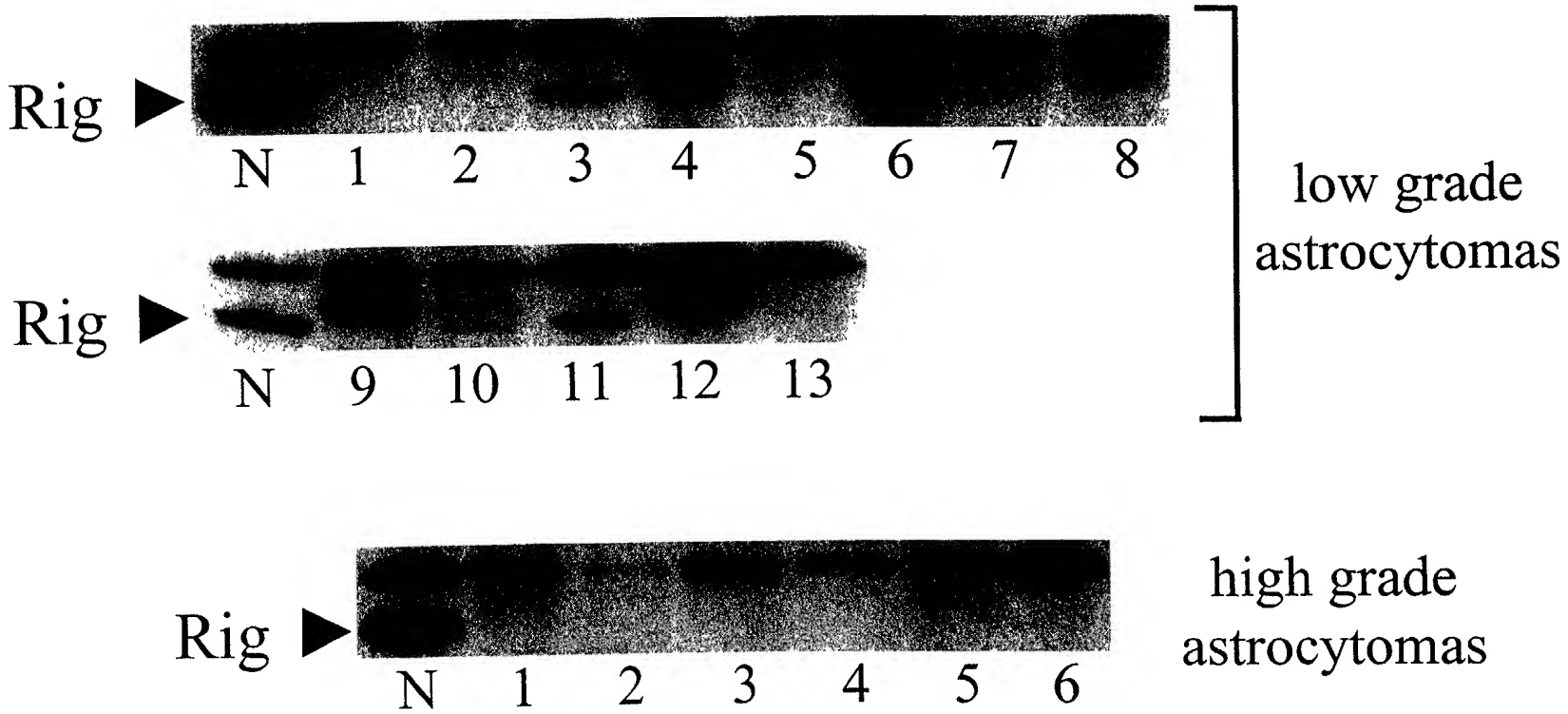


Figure 13

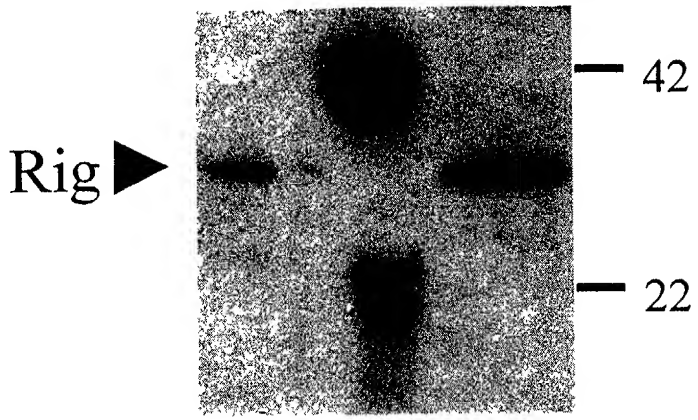


Figure 14

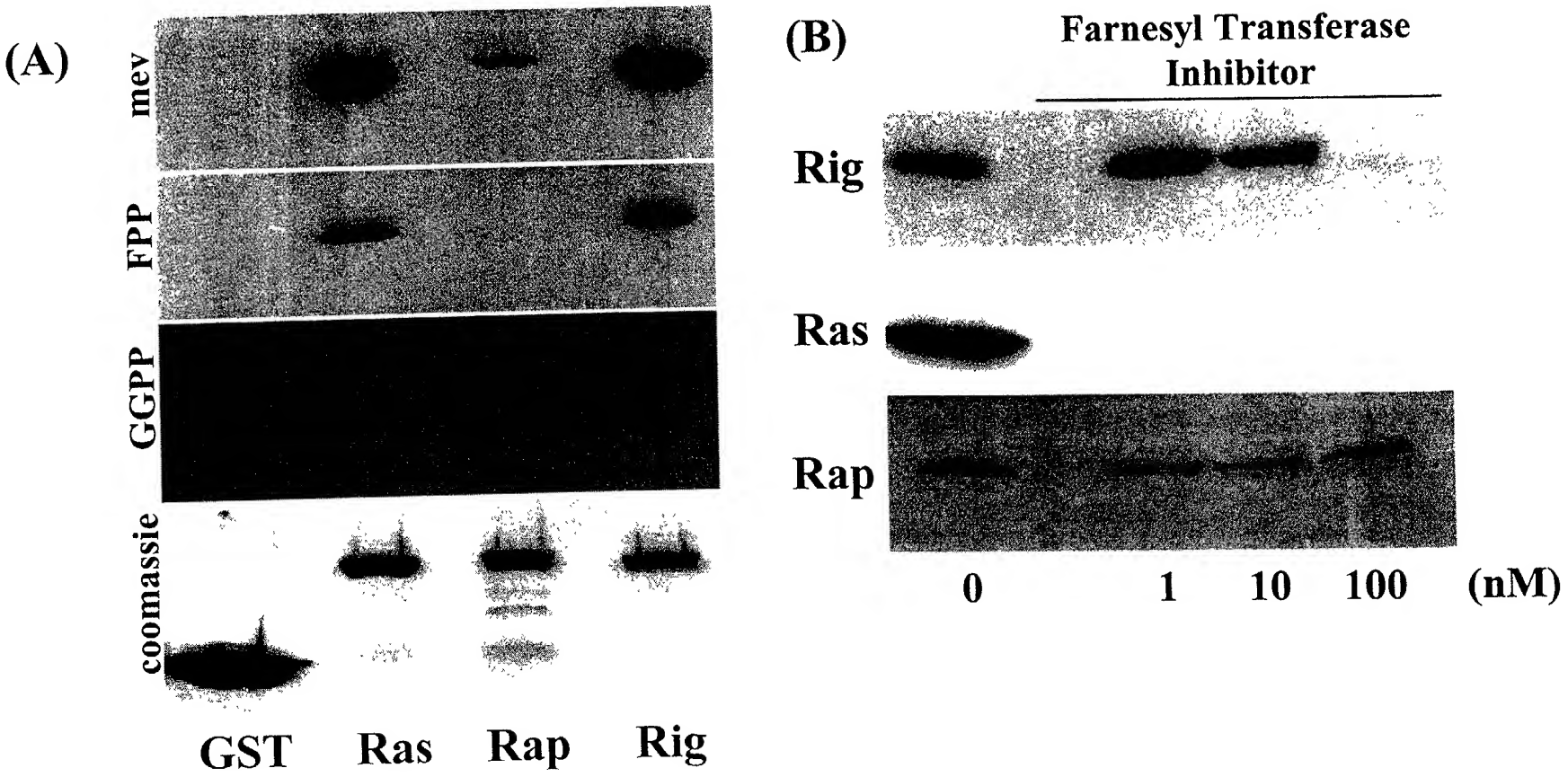


Figure 15